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Burden of digestive diseases in Portugal:

Trends in hospitalizations over the last decade

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Ao futuro vindouro!

Abstract

OBJECTIVE: Data on gastrointestinal diseases' burden is incomplete, particularly in Southern European countries. The aim of this study was to estimate the burden of digestive diseases in Portugal.

METHODS: Retrospective observational study based on the national hospitalizations database, identifying all consecutive episodes with a first diagnosis of a digestive disease between 2000 and 2010, using ICD-9-CM codes. Comparative analyses were performed to assess hospitalization trends of major indicators over time and across regions.

RESULTS: More than 75,000 deaths attributable to digestive diseases were observed, representing 16% of the overall in-hospital mortality. Over half of these (59%) were premature deaths (below 75 years). Biliary-tract disease was the most common digestive disorder leading to hospitalization (249,817 episodes, 5,210 episodes of acute stone-related cholecystitis in 2010 with 11% increase compared to 2000). Gastric cancer was responsible for the highest number of in-hospital deaths (10,278) and alcohol-related liver disorders accounted for the highest in-hospital premature deaths (7,572). Charges and in-hospital mortality rate for major digestive diseases both showed a significant positive relation with time progression ($\beta=0.195$, $p<0.001$), however, when adjusted for age, this was not significant. Significant positive associations were found between age and in-hospital mortality (odds ratio=1.032, $p<0.001$) and between charges and in-hospital mortality (odds ratio=1.054, $p<0.001$).

CONCLUSION: In Portugal, digestive diseases represent an important burden with evidence of increasing trend. Ageing population strongly contributes to this increase, setting further demands on healthcare organizations. Diseases such as gastric cancer, biliary-tract disease and alcohol-related liver disorders may require particular attention.

KEY WORDS: Digestive diseases, burden of illness, administrative data, mortality.

Resumo

INTRODUÇÃO: Existem poucos dados sobre o *burden* das doenças digestivas, nomeadamente em países sul-europeus.

OBJECTIVOS: O objectivo deste estudo foi estimar o *burden* das doenças digestivas em Portugal.

MÉTODOS: Estudo observacional retrospectivo com base no registo nacional de internamentos (base de dados GDH – ACSS), identificando todos os episódios consecutivos com diagnóstico principal correspondente a doença digestiva entre 2000 e 2010, usando os códigos ICD-9-CM. Foi feita uma análise comparativa para estudar as tendências dos internamentos ao longo do tempo e através das regiões geográficas.

RESULTADOS: Foram observadas mais de 75,000 mortes atribuíveis a doenças digestivas, representando 16% da mortalidade global intra-hospitalar. Mais de metade destas (59%) foram mortes prematuras (abaixo dos 75 anos de idade). A doença do tracto biliar foi a condição que conduziu mais frequentemente a internamento (249,817 episódios, 5,210 episódios de colecistite aguda em 2010 com um aumento de 11% em relação a 2000). O cancro gástrico foi responsável pelo maior número de mortes intra-hospitalares (10,278) e a doença hepática alcoólica pelo maior número de mortes intra-hospitalares prematuras (7,572). Os custos e a taxa de mortalidade intra-hospitalar para as principais doenças digestivas mostraram uma relação positiva com a evolução temporal anual ($\beta=0.195$, $p<0.001$), no entanto após ajuste para a idade, esta relação não foi significativa. Foi encontrada associação positiva significativa entre a idade e a taxa de mortalidade intra-

hospitalar (odds ratio= 1.032, p< 0.001) e entre os custos e a taxa de mortalidade intra-hospitalar (odds ratio= 1.054, p< 0.001).

DISCUSSÃO: Em Portugal, as doenças digestivas representam um *burden* importante, com evidência de tendência crescente. O envelhecimento populacional contribui significativamente para este aumento, produzindo desafios adicionais no futuro da organização dos cuidados de saúde. Doenças como cancro gástrico, doença do tracto biliar e doença hepática alcoólica podem vir a requerer particular atenção.

PALAVRAS CHAVE: Doenças digestivas, *burden* de doença, dados administrativos, mortalidade.

Preamble

Medicine is a science of uncertainty and an art of probability.
William Osler (1849–1919)

A Medicina Interna é uma especialidade médica com vertente assistencial diversificada e complexa, mas também integradora e resolutiva. Exerce em diferentes sectores hospitalares e responde a estados variados de gravidade clínica.

Desde cedo me prendeu a atenção o *peso* dos doentes hepáticos crónicos nas enfermarias hospitalares. Tantas vezes jovens, gravemente doentes, com internamentos prolongados e não raramente outcomes adversos.
Foi esta observação que esteve na base do estudo da presente dissertação.

Dessa observação até à presente dissertação vai um caminho feito de tempo, de conselhos, de trabalho em equipa, de contratempo, de escolhas, de perspectiva, de reestruturação.

O conceito de *burden of illness* abrange vários aspectos relativos ao impacto das doenças nos indivíduos e nas populações – frequência, incidência e prevalência, mortalidade, mortalidade prematura, anos de vida perdidos, morbilidade, vivência com incapacidade, custos directos e indirectos.

Este trabalho reflecte uma aproximação a esse conceito de *burden*, que se afigura como um conceito de grande utilidade e importância para a compreensão dos padrões de doença e sua evolução, e nomeadamente na resposta ao desafio que é a adaptação dos sistemas de saúde a esta evolução de padrões.

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Acronyms and abbreviations

ACSS: Administração Central dos Serviços de Saúde (Central Administration of Health System of the Portuguese Ministry of Health)
CCS: Clinical classification software
DRG: Diagnosis related groups
DD: digestive diseases
DALY's: disability adjusted life years
EUR: euros
GI: gastro-intestinal
IBD: Inflammatory bowel disease
IBM SPSS Statistics v20™: Statistical Package for Social Sciences
ICD-9-CM: International Classification of Diseases - 9th Revision - Clinical Modification
INE: Instituto Nacional de Estatística (National Institute of Statistics)
LOS: length of stay
NAFLD: nonalcoholic fatty liver disease
NHS: Serviço Nacional de Saúde (National Health Service)
NUTS: Nomenclature of Units for Territorial Statistics
PYLL: potential years of life lost
UK: United Kingdom
USA: United States of America
WHO: World Health Organization
YLL: years of life lost

1. Introduction

Digestive diseases (DD) have a great impact on population health and well-being. In the USA their global burden has been systematically assessed, representing high mortality (responsible for 10% of overall mortality in 2009[1]) and significant costs (142 millions of dollars in 2004[2]). There are other studies focusing on DD global impact in national health systems (USA, Eastern countries and UK)[1-8], with variation in measurements and reporting.

In Europe, diarrhoeal diseases, hepatitis B and C, intestinal nematode infections, gastrointestinal (GI) cancer, liver cancer, pancreatic cancer and specific digestive diseases (peptic ulcer, liver cirrhosis, appendicitis) represented almost 30 million disability-adjusted life years (DALYs= years of life lost *plus* years lived with disability*)* in 2011, according to WHO[9]. Some studies addressed the burden of a group of digestive disorders in Europe (liver disease[10], GI and liver cancers[11], hepatitis C virus[12] and inflammatory bowel disease[13]). In southern European countries there are national reports highlighting epidemiological trends in specific group of digestive diseases such as upper gastrointestinal bleeding, gastro-oesophageal reflux, Barrett's oesophagus, inflammatory bowel disease or celiac disease (e.g.[14-22]), but only two studies addressed their global burden[23, 24].

Additionally, according to the latest WHO report on World Health Statistics[25], among the first listed diseases responsible for years of life lost (YLL) and premature mortality, two digestive disorders were identified: diarrhoeal diseases in 5th place and cirrhosis in 17th place.

Studies addressing disease morbidity and mortality are important not only for clinicians and researchers, but also for health policy advising, leading to health care improvement.

Despite limitations of working with administrative databases, with possible coding inaccuracies and limited clinical data, these databases can be used to study healthcare outcomes, monitor population health status and have the potential to contribute to quality development in healthcare[26-31]. These administrative databases are easily available, have a national coverage, are relatively inexpensive and can be useful for identifying long-term trends in hospital care, analysing quality and performance indicators, and studying the relation between hospitalizations and environmental determinants[32-34]. In Portugal, all hospitals of the National Health Service have this mutual national hospitalization database in use since 1990.

Therefore, we aimed to study the global burden of digestive diseases in a Southern European country, by analysing associated hospitalizations, mortality and monetary costs.

2. Material and Methods

Study design and data source

We conducted a retrospective observational study using data from the national hospitalizations database. This database, provided by the Central Administration of Health System of the Portuguese Ministry of Health (ACSS), gathers administrative and clinical data concerning hospitalization (in-patient and ambulatory surgery) episodes in National Health Service hospitals, notably diagnoses and procedures performed during hospital stay. Diagnosis and procedures are coded using the International Classification of Diseases - 9th Revision - Clinical Modification (ICD-9-CM). In Portugal, the ICD-9-CM based Diagnosis Related Group (DRG) prospective payment system is in use since 1990.

Study population

We studied all consecutive in-patient episodes in public hospitals between January 1st, 2000 and December 31st 2010 with a principal diagnosis corresponding to a digestive disease - any disorder affecting the alimentary tract and its associated organs: liver, gallbladder and pancreas. Data from private hospitals, representing around 15% of all inpatient stays in Portugal[29], was not available for inclusion in this study.

Patients of all ages were considered and all consecutive episodes analyzed. Readmissions were considered as independent episodes. The analysis of database information maintained patient anonymity.

Data collection and variables estimate

For each identified hospitalization episode, the following variables were analyzed: age, gender, length of stay (LOS), principal and secondary diagnoses (coded according to ICD-9-CM), discharge status (to compute

in-hospital mortality), mean monetary charges, type of admission, and discharge date.

Because the list of ICD-9-CM codes is extensive, containing over 14,000 diagnosis codes and 3,900 procedure codes, we used the Agency for Healthcare Research and Quality's (AHRQ) Clinical Classification Software (CCS) to summarize ICD-9-CM codes into a small number of clinically meaningful groups[35].

We selected all CCS categories corresponding to diagnostic entities of digestive diseases. Categories were screened and ICD-9-CM codes within each category reviewed, in order to avoid inclusion of non-digestive diseases or symptoms with probable association with other type of disorders. One CCS category was found to include only a limited number of digestive diagnoses, and so this specific category (CCS 663 Screening and history of mental health and substance abuse codes) was partially adapted, comprising ICD-9-CM codes exclusively related to alcoholic digestive diseases.

When studying contribution of specific diseases, some ICD-9-CM codes were selected and organized within groups in order to emphasize clinical and epidemiological relevant data.

Healthcare costs for hospitalizations attributable to GI diseases were calculated according to the expenditure tables for NHS hospital reimbursements. The reimbursement is made according to the diagnosis-related groups (DRGs) based budget allocation model. Expenditure tables are defined by governmental ordinance (in *Diário da República*).

Demographic characteristics such as population size and its annual variations were obtained from the National Institute of Statistics (INE).

Analysis

Descriptive and inferential statistical analyses were performed using IBM SPSS Statistics v20™ (Statistical Package for Social Sciences).

Analysis of mortality indicators included: in-hospital death (death during hospitalization episode), in-hospital premature death (death during hospitalization episode in patient having 75 years or less), PYLL (total potential years of life lost by population under age 75), in-hospital mortality rate (proportion of episodes with a particular condition with an outcome of death from that condition). Formulas as follows:

- Hospitalization rate=

$$\frac{number\ of\ patients\ hospitalized\ for\ disease\ x}{total\ population} \times 100.000$$

- In-hospital deaths for disease x (%)=

$$\frac{number\ of\ patients\ dying\ with\ disease\ x}{total\ of\ hospitalizations\ with\ disease\ x} \times 100$$

- In-hospital premature deaths for disease x (%)=

$$\frac{number\ of\ patients\ dying\ with\ disease\ x\ under\ the\ age\ of\ 75}{total\ number\ of\ inhospital\ deaths\ with\ disease\ x} \times 100$$

- PYLL rate=

$$\frac{sum\ of\ the\ total\ PYLL\ of\ patients\ with\ less\ than\ 75\ years\ dying\ with\ disease\ x}{total\ of\ hospitalizations\ with\ less\ than\ 75\ years} \times 100.000 =$$

$$= \frac{\Sigma\,(75 - age\ of\ death*)}{total\ of\ hospitalizations\ with\ less\ than\ 75\ years} \times 100.000$$ (* if death at age » 75, equals Ø)

Comparative analysis of indicators in 2000 and 2010 was performed in order to assess changes over time. Chi-square test was used with a statistical significance level set at $p< 0.05$. Linear regression models were performed to assess trends in hospitalization rate, monetary charges and in-hospital mortality rate, studying their relationship with time progression. To adjust mean charges and in-hospital mortality rate for age, we included this last variable as independent variable. To understand the association between age, charges and in-hospital mortality we performed a logistic regression, using in-hospital mortality as dependent variable and the other two variables as independent. In all these regressions, charges were studied in millions of Euros.

Geographic distribution of hospitalization rate (number of episodes per 100.000 inhabitants) and in-hospital mortality (with age-sex direct standardization of mortality for the 2011 Portuguese population) was made using the NUTS II and III classification for Portugal (Nomenclature of Units for Territorial Statistics levels II and III).

3. Results

During the decade period 2000-2010, there were over 10.5 million registered hospitalizations in Portuguese public hospitals. Of these, we identified almost 1.5 million episodes with a principal diagnosis of a DD (13.8 % of total).

CCS categories: outline of all digestive diseases

An overview of all CCS categories that we have considered as digestive diseases is presented in Table 1, regarding frequency, age, LOS, costs and mortality.

The most common diagnosis for in-hospital stay was biliary tract disease with almost 250,000 hospitalizations, followed by abdominal hernia and appendicitis/appendiceal conditions. Among the first ranked DD's we also have pancreatic disorders, alcohol-related GI diseases and GI bleeding.

The median LOS for patients with digestive diseases was 4 days, with the following disorders sharing the highest LOS (11 days): cancer (gastric, pancreatic, small intestine/gallbladder/peritoneal) and non-malignant condition peritonitis/intestinal abscess.

Patients with digestive congenital anomalies and intestinal infection presented with the lowest mean age, while patients with malignant conditions (colon, pancreatic, rectal/anal, small intestine/gallbladder/peritoneal and gastric cancers) and non-malignant disorders such as gastrointestinal hemorrhage and diverticular disease present with the highest age.

Liver/intrahepatic bile duct cancer and gastric cancer were responsible for the highest mean monetary charges (7,168 € and 6,422 €, respectively).

In terms of mortality, during this decade, digestive diseases were responsible for more than 75,000 in-hospital deaths, corresponding to

15.8% of the overall in-hospital mortality. More than half of these (59%) were premature deaths, leading to a PYLL rate of 49,663 per 100,000 population under 75 years of age.

The principal cause of in-hospital deaths among patients with digestive diseases was gastric cancer with more than 10,000 losses during this decade. For patients dying prematurely, the leading cause was alcoholic-related liver disease, responsible for more than 7,500 deaths.

Comparing indicators in digestive conditions versus the sum of all clinical conditions, we observe that the mean age is slightly higher in patients presenting with digestive diseases (53.3 ± 24.4 vs 46.1 ± 28 yrs), the mean monetary charges are more elevated (3.157 vs 2.494 EUR) and in-hospital mortality rate, in-hospital premature deaths and rate of PYLL's are all higher (5.17% vs 4.51%, 58.7% vs 46.2%, 49,663 vs 36,905) in DD's when compared with the total of all diseases.

Table 1: Gastrointestinal and Hepatology Principal Discharge Diagnoses for Hospitalizations, using CCS, 2000-2010 (only inpatient data)

Rank among GI dx	Rank among all dx	Single-Level CCS principal diagnosis code and category	Total No. discharges	Median LOS (days)	Mean age (SD)	Mean charges (EUR)	In-hospital deaths, n (%)	In-hospital premature deaths, n (%)	Rate of PYLL[75]
1	5	149 - Biliary tract disease	249,817	4	60.8 (17.2)	2,447	3,673 (1.47)	1,137 (31.0)	5,421
2	6	143 - Abdominal hernia	240,472	2	55.5 (20.7)	2,157	1,466 (0.61)	481 (32.8)	2,258
3	16	142 - Appendicitis and other appendiceal conditions	121,917	3	28.3 (19.0)	2,257	302 (0.25)	126 (41.7)	1,174
4	43	152 - Pancreatic disorders (not diabetes)	66,128	7	61.2 (18.5)	3,036	3,045 (4.60)	1,388 (45.6)	39,395
5	44	663 partial - considering only related GI diseases ICD-9-CM codes: 535.3x, 571.0, 571.1, 571.2, 571.3 (alcoholic gastritis and alcoholic related liver disorders)	63,351	8	57.5 (12.4)	5,439	8,751 (13.8)	7,572 (86.5)	222,282
6	48	153 - Gastrointestinal hemorrhage	59,753	6	66.9 (18.7)	2,921	4,625 (7.74)	1,652 (35.7)	54,325
7	51	135 - Intestinal infection	57,409	3	21.7 (29.8)	1,424	777 (1.35)	213 (27.4)	4,259
8	52	14 - Colon cancer	57,024	10	69.2 (12.0)	6,129	8,949 (15.69)	4,995 (55.8)	140,985
9	54	154 - Noninfectious gastroenteritis	53,442	2	21.9 (30.1)	1,260	624 (1.17)	167 (26.8)	4,119
10	61	13 - Gastric cancer	47,331	11	67.8 (13.1)	6,422	10,278 (21.72)	6,333 (61.6)	252,763
11	67	147 - Anal and rectal conditions	44,564	2	48.5 (17.4)	2,230	209 (0.47)	110 (52.6)	3,051
12	68	145 - Intestinal obstruction without hernia	44,519	6	63.1 (21.9)	3,163	3,422 (7.69)	1,433 (41.9)	58,742
13	70	15 - Rectal and anal cancer	41,735	10	68.5 (12.1)	5,890	5,097 (12.21)	3,038 (59.6)	121,063
14	86	151 - Other liver diseases	34,776	6	57.9 (17.4)	5,569	3,988 (11.47)	3,055 (76.6)	173,510
15	91	155 - Other gastrointestinal disorders	32,895	6	54.7 (25.8)	3,549	1,444 (4.39)	712 (49.3)	36,100
16	106	120 - Hemorrhoids	25,965	2	51.5 (14.4)	2,172	24 (0.09)	16 (66.7)	719
17	107	146 - Diverticulosis and diverticulitis	25,631	7	66.1 (15.1)	2,905	640 (2.50)	149 (23.3)	6,141
18	123	138 - Oesophageal disorders	19,899	4	48.1 (30.4)	3,047	406 (2.04)	196 (48.3)	18,394
19	126	251 - Abdominal pain	19,481	2	41.4 (26.8)	1,171	306 (1.57)	107 (35.0)	8,246
20	132	141 - Other disorders of stomach and duodenum	18,706	2	28.1 (31.8)	2,109	346 (1.85)	167 (48.3)	11,326
21	137	6 - Hepatitis	18,415	2	44.1 (18.4)	3,502	400 (2.17)	291 (72.8)	30,991
22	140	144 - Regional enteritis and ulcerative colitis	17,470	8	39.7 (18.1)	3,272	195 (1.12)	119 (61.0)	13,074
23	143	17 - Pancreatic cancer	17,109	11	68.8 (12.5)	5,161	4,931 (28.82)	3,054 (61.9)	298,525
24	152	18 - Other GI organs and peritoneal cancer	15,257	11	68.0 (14.4)	5,350	3,207 (21.02)	1,864 (58.1)	212,684
25	154	140 - Gastritis and duodenitis	14,921	5	61.1 (25.1)	2,454	347 (2.33)	106 (30.5)	13,130
26	158	139 - Gastroduodenal ulcer (except hemorrhage)	14,051	8	60.8 (19.0)	6,137	1,063 (7.57)	422 (39.7)	47,475
27	164	16 - Liver and intrahepatic bile duct cancer	12,988	7	64.9 (14.1)	7,168	3,301 (25.42)	2,424 (73.4)	300,681
28	173	12 - Osophageal cancer	11,912	9	63.2 (12.3)	5,049	2,596 (21.79)	2,065 (79.5)	319,925
29	207	148 - Peritonitis and intestinal abscess	6,569	11	57.0 (18.9)	4,679	1,002 (15.25)	660 (65.9)	187,615
30	212	214 - Digestive congenital anomalies	5,895	4	11.1 (21.4)	5,400	52 (0.88)	45 (86.5)	45,342
		Total digestive diseases	1,459,402	4	53.3 (24.4)	3,157	75,466 (5.17)	44,265 (58.7)	49,663
		Total diseases	10,586,118	4	46.1 (28.0)	2,494	477,702 (4.51)	220,623 (46.2)	36,905

Major digestive disorders: trends over time

Table 2 shows the five main groups of digestive diseases, according to organ or type of disorder: biliopancreatic, liver, cancers, inflammatory bowel disease and GI infections. The contribution of each group is represented, as well as comparison of indicators over time.

Selected diseases within these five groups represent 4.7 % of the overall hospitalizations in 2010 (42,719 episodes).

Within the group of patients presenting with biliopancreatic diseases, acute pancreatitis accounts for the highest rate of hospitalization (53.9 hospitalizations per 100.000 inhabitants). Comparative changes between 2000 and 2010 regarding total number of hospitalizations show that cholangitis is responsible for the highest increase (178.8%, $p< 0.001$) and chronic pancreatitis for the highest decrease (-19.8%, $p= 0.023$). In-hospital deaths were higher in 2010 for acute conditions (cholelithiasis with acute cholecystitis, cholangitis and acute pancreatitis), when compared to 2000, although with no significant statistical difference.

Concerning patients with liver diseases, alcohol-related disorders show the leading rate of hospitalization, while viral hepatitis B and C show an important decline (-65.1% and -57.1% respectively, $p < 0.001$). Cirrhosis-related complications (hepatic encephalopathy, portal hypertension, ascites, oesophageal varices rupture, spontaneous bacterial peritonitis, hepatorenal and hepatopulmonary syndromes) were not only responsible for an increase of 41.3% in hospitalizations over the decade ($p< 0.001$), but for the highest in-hospital mortality rate within this group both in 2000 and in 2010 (14.4% and 16.8% respectively). The liver diseases group was the only one of digestive diseases in which in-hospital mortality rate increased across all disorders, and it is the most frequent secondary-diagnosis (total 22,901 episodes).

Digestive cancers show a global increase in hospitalization rates except for oesophageal (-14.7%, $p= 0.008$), gastric (-9.7%, $p= 0.006$) and rectal/anal cancers (-5.6%, $p< 0.001$). All the others have increasing hospitalization rates over the decade, led by liver and intra-hepatic bile duct cancer (91.2% increase, $p< 0.001$). The main causes of in-hospital deaths and in-hospital mortality rates among digestive diseases belong to this group (pancreas, stomach, colon, gallbladder and extra-hepatic bile ducts, oesophagus, liver and intra-hepatic bile duct). Regarding evolution of mortality indicators within this group, we observe that three conditions presented a decline in hospital mortality rates, despite having

higher number of hospitalizations: liver and intrahepatic bile duct cancer, small intestine cancer and retroperitoneal/peritoneal cancer. In 2010, all other digestive cancers presented higher in-hospital mortality rates than in 2000.

With regards to inflammatory bowel disease (IBD), there has been a much larger increase in the rate of hospitalizations per 100,000 population rate for Crohn's disease than ulcerative colitis (UC) (30.1% vs 9.6%, with $p= 0.029$) . UC has shown a decrease in mortality indicators, notably in-hospital mortality rate changed from 3.1 in 2000 to 0.4 in 2010 ($p= 0.001$), which was not observed in Crohn's disease.

For the last group, patients with GI infections, all disorders show a statistical significant declining trend in hospitalization rates, with more pronounced decline in food born infections (-94.6%), followed by atypical infections like cholera, typhoid fever and amebiasis (-75.2%). Despite this decline, in-hospital deaths, as well as in-hospital mortality rate, were higher in 2010 when compared with 2000 for infectious colitis, enteritis and gastroenteritis (24 in-hospital deaths and 0.9% of in-hospital mortality rate in 2000 vs 75 and 3.2% in 2010, $p< 0.001$).

Overall, for the five considered main groups of digestive diseases, hospitalization rates increased 4.3% ($p< 0.001$). Median LOS decreased for all listed disorders except for non-alcoholic fatty liver disease (NAFLD), colitis/enteritis/gastroenteritis of infectious origin and GI food born infections. Total monetary charges increased (global 17.2%) except for chronic pancreatitis, viral hepatitis B and C, NAFLD, oesophageal and gastric cancer, and almost all GI infections. The most substantial increases in total charges were attributable to cholangitis (202.0%) and liver/intrahepatic bile duct cancer (119.5%); most significant decrease was observed in food born GI infections (-93.0%) and viral hepatitis B (-70.2%).

Number of in-hospital deaths increased from 4,265 in 2000 to 5,239 in 2010, and also in-hospital mortality rate rose from 10.4% in 2000 to 12.3% in 2010 ($p< 0.001$).

Mean age of hospitalized patients rose from 57.5 years in 2000 to 62.4 years in 2010.

To complement these results and more accurately predict the relationship between indicators and time, we used linear regression models to assess trends concerning three key indicators: hospitalization rates, monetary charges and in-hospital mortality rates. Table 3 includes all detailed annual data. Hospitalization rates show no significant relation with time (β=0.155, p= 0.870). In-hospital mortality rate showed a significant positive relation with time progression (while monetary charges and in-hospital mortality rate both show an important relation (β=0.195, p<0.001). However, when adjusted for age, this relation was not significant (discharge year: β=0.152, p= 0.141; age: β=0.089, p= 0.649). Mean monetary charges also showed a significant positive relation with time progression (β=0.058, p<0.001). However, when adjusted for age, this relation was not significant (β=0.024, p= 0.064). In this linear regression, age showed a significant positive relation with mean monetary charges (β=0.071, p= 0.014), even when adjusted for time progression.

Significant positive associations were found between age and in-hospital mortality (odds ratio=1.032, p<0.001) and between monetary charges and in-hospital mortality (odds ratio=1.054, p<0.001).

Table 2 – Gastrointestinal and Hepatology Selected Discharge Diagnoses for Hospitalizations in 2010 (only inpatient data)

Principal diagnosis	Total nr. discharges in 2010	Total nr. discharges per 100.000 inhabitants	% Change from 2000 (p-value *)	Median LOS (days), 2010 (2000)	% Total hospital days within all hospitalizations **	Total charges (EUR, millions)	% Change from 2000	In-hospital deaths in 2010, n (%)	In-hospital deaths in 2000, n (%)	p-value (*)	% Planned admissions, 2010 (2000)	Mean age, 2010 (2000)	Total nr. discharges as a secondary diagnosis***
Biliopancreatic diseases													
Cholelithiasis with acute cholecystitis	5,210	51.8	11.2 (< 0.001)	7.0 (7.0)	0.667	14,146	17.4	151 (2.9)	111 (2.4)	0.101	7.2 (10.0)	65.8 (63.8)	529
Cholangitis	1,263	12.6	178.8 (< 0.001)	8.0 (8.0)	0.199	4,222	202.0	78 (6.2)	25 (5.5)	0.614	8.6 (15.9)	69.6 (65.7)	1,037
Acute pancreatitis	5,426	53.9	13.3 (< 0.001)	7.0 (8.0)	0.803	16,305	14.9	250 (4.6)	219 (4.6)	0.932	2.1 (2.6)	62.9 (60.5)	1,010
Chronic pancreatitis	296	2.9	-19.8 (0.023)	6.0 (7.0)	0.037	982	-14.6	5 (1.7)	7 (1.9)	0.841	25.7 (31.2)	54.9 (49.4)	458
Cyst and pseudocyst of pancreas	212	2.1	15.8 (0.059)	7.0 (13.0)	0.034	916	2.5	3 (1.4)	13 (7.1)	0.004	53.3 (36.6)	56.6 (55.5)	321
Liver diseases													
Viral hepatitis B	185	1.8	-65.1 (< 0.001)	1.0 (6.0)	0.018	644	-70.2	4 (2.2)	5 (0.9)	0.200	51.4 (30.9)	43.7 (37.5)	1,487
Viral hepatitis C	359	3.6	-57.1 (< 0.001)	1.0 (1.0)	0.028	2,106	-16.1	10 (2.8)	3 (0.4)	< 0.001	53.8 (67.5)	48.6 (37.7)	4,222
Alcohol-related liver diseases	4,711	46.8	-17.7 (< 0.001)	7.0 (9.0)	0.739	28,543	2.6	714 (15.2)	744 (13)	0.002	15.0 (11.1)	58.6 (56.8)	6,069
NAFLD	188	1.9	-20.7 (0.005)	3.0 (2.0)	0.017	678	-13.2	12 (6.4)	9 (3.8)	0.222	43.9 (57.0)	55.7 (49.9)	2,672
Cirrhosis-related complications	1,164	11.6	41.3 (< 0.001)	7.0 (7.0)	0.166	4,742	44.3	196 (16.8)	119 (14.4)	0.149	5.8 (12.0)	60.6 (56.9)	8,451
Digestive cancers													
Oesophageal cancer	965	9.6	-14.7 (0.008)	8.0 (10.0)	0.188	5,078	-9.9	216 (22.4)	214 (18.9)	0.050	43.1 (49.4)	62.8 (63.2)	766
Gastric cancer	3,999	39.8	-9.7 (0.006)	10.0 (12.0)	0.851	26,313	-3.8	926 (23.2)	865 (19.5)	< 0.001	48.8 (43.3)	68.7 (67.1)	1,594
Colon cancer	5,677	56.4	31.8 (< 0.001)	10.0 (11.0)	1.113	35,979	43.1	895 (15.8)	636 (14.8)	0.172	52.5 (44.0)	70.1 (68.0)	1,974
Rectal and anal cancer	3,569	35.5	-5.6 (0.546)	10.0 (11.0)	0.737	22,007	5.7	474 (13.3)	421 (11.1)	0.005	62.6 (58.7)	69.0 (67.6)	1,384

Liver and intrahepatic bile duct cancer	1,748	17.4	91.2 (< 0.001)	5.0 (9.0)	0.239	12,773	119.5	380 (21.7)	243 (26.6)	0.005	50.9 (32.9)	64.8 (62.5)	637
Gallbladder /extra-hepatic bile ducts cancer	972	9.7	21.0 (0.002)	11.0 (14.0)	0.222	5,300	28.7	220 (22.6)	160 (19.9)	0.166	30.8 (27.0)	71.6 (69.2)	303
Pancreatic cancer	1,816	18.1	32.9 (< 0.001)	10.0 (12.0)	0.355	9,456	37.4	530 (29.2)	353 (25.8)	0.037	31.9 (27.7)	69.4 (67.8)	554
Small intestine cancer	235	2.3	41.6 (< 0.001)	10.0 (13.5)	0.053	1,479	52.8	44 (18.7)	32 (19.3)	0.889	41.7 (37.3)	65.9 (63.7)	82
Retroperitoneal and peritoneal cancer	246	2.4	15.5 (0.045)	8.0 (10.0)	0.049	1,387	44.0	42 (17.1)	39 (18.3)	0.729	62.6 (52.6)	61.4 (58.1)	155
Inflammatory bowel disease													
Chron's disease / granulomatous enteritis	1,189	11.8	30.1 (< 0.001)	7.0 (7.0)	0.175	4,168	45.8	8 (0.7)	5 (0.5)	0.715	27.0 (36.7)	37.3 (37.0)	957
Ulcerative colitis	492	4.9	9.6 (0.039)	8.0 (11.0)	0.085	1,422	3.7	2 (0.4)	14 (3.1)	0.001	23.0 (27.4)	45.1 (46.6)	572
GI infections													
Colitis, enteritis and gastroenteritis of infectious origin	2,379	23.7	-12.2 (0.002)	3.0 (2.0)	0.167	3,825	11.1	75 (3.2)	24 (0.9)	< 0.001	1.3 (1.1)	35.6 (20.8)	735
Salmonella gastroenteritis	226	2.2	-51.1 (< 0.001)	5.0 (5.0)	0.022	439	-42.4	1 (0.4)	1 (0.2)	0.605	5.3 (1.1)	26.3 (14.3)	38
Bacterial enteritis	146	1.5	-52.0 (< 0.001)	3.0 (3.0)	0.010	231	-43.8	1 (0.7)	1 (0.3)	0.595	0.7 (0.0)	23.2 (7.0)	21
Atypical (cholera, typhoid fever, amebiasis, other protozoal)	32	0.3	-75.2 (< 0.001)	6.0 (8.0)	0.004	91	-61.6	1 (3.1)	2 (1.6)	0.555	6.3 (4.7)	36.5 (36.6)	54
Food born	14	0.1	-94.6 (< 0.001)	4.5 (2.0)	0.001	27	-93.0	1 (7.1)	0 (0)	< 0.001	0.0 (0.8)	46.0 (19.1)	13
Total	42,719	424.7	4.3 (< 0.001)	8.0 (8.0)	6.980	203,260	17.2	5239 (12.3)	4,265 (10.4)	< 0.001	28.1 (25.9)	62.4 (57.5)	23,323

* Pearson chi-square test

** All hospitalizations corresponds to 909,380 episodes

*** excluding episodes with such a code in the principal diagnosis

Table 3 - Hospitalization rate, in-hospital mortality rate and total charges for major digestive diseases in Portugal from 2000 to 2010.

Year	Hospitalization rate (per 100,000 inhabitants)	In-hospital mortality rate (%)	Total charges (€, millions)
2000	416	10.4	173.40
2001	430	10.9	181.17
2002	427	11.1	185.85
2003	438	10.7	191.96
2004	441	11.1	194.65
2005	441	11.4	196.50
2006	438	11.6	198.49
2007	438	12.0	202.21
2008	436	12.2	206.23
2009	417	12.4	201.49
2010	425	12.3	203.25

Geographical variations

Figure 1 shows the geographic distribution of hospitalization rate (number of episodes per 100,000 inhabitants) and in-hospital mortality rate (number of deaths per total of hospitalizations) in 2000 and 2010 for all digestive diseases. Tâmega, Alentejo Litoral and Entre Douro e Vouga were the 3 regions with the lowest hospitalization rates both in 2000 and 2010. North interior comprised regions with the highest rates of hospitalization. In-hospital mortality rate was higher in Algarve in 2000, but in contrast North and Alentejo presented with higher in-hospital mortality rates in 2010.

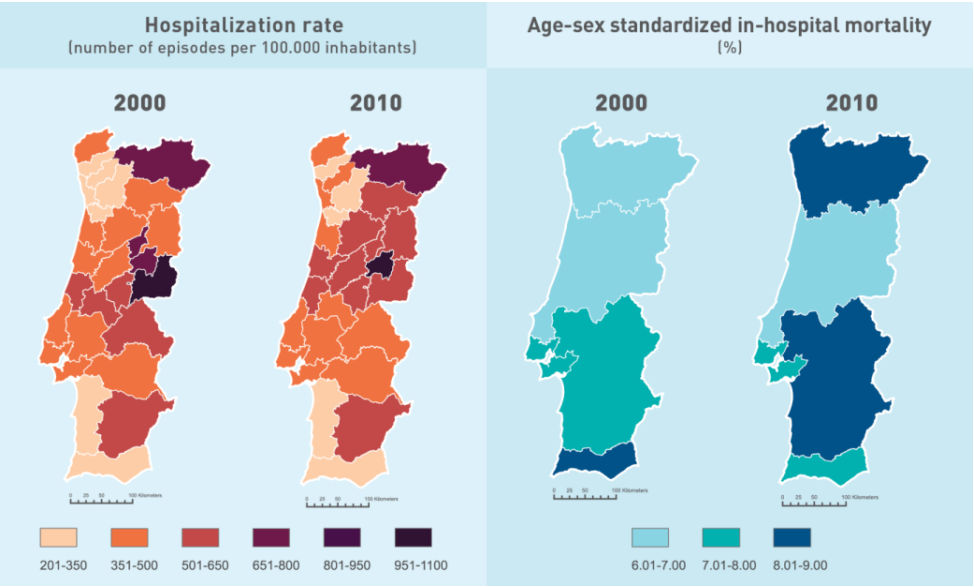

Figure 1: Geographical distribution of hospitalization rate (number of episodes per 100,000 inhabitants) and in-hospital mortality (%) for major digestive diseases, in Portugal, from 2000-2010.

4. Discussion

Key evidence – analyzing main findings

Studies reporting the incidence, prevalence and mortality of specific digestive diseases in particular regions or countries are often published. Also, in times of overt financial constraints, studies on economic impact of diseases are increasingly more frequent. However, studies assessing the global impact of digestive diseases in individuals, society and health systems are scarce, as well as reports on its variations and trends[8]. Other studies on this subject have been discussed already[1, 2, 3, 5, 6], coming mostly from USA and less from Europe[8, 23, 24], both including data from outpatient visits and inpatient hospital admissions. In southern European countries there is particular need of reporting, because of the lack of studies addressing this subject[23, 24].

The growing burden of digestive diseases observed in our study is consistent with the findings in these other reports, however the trends in specific disorders are somewhat different.

In the UK, conditions such as hepatitis C infection, acute and chronic pancreatitis, alcoholic liver disease, gallstone disease, upper gastrointestinal haemorrhage, diverticular disease, Barrett's oesophagus, and oesophageal and colorectal cancers are drawing attention for increasing incidence and thus future implications[8]. In USA, gastroesophageal reflux, acute pancreatitis, colorectal cancer and *clostridium difficile* infections are the leading reasons for concern according to Peery *et al*[1]. Everhart *et a*l[2] highlighted digestive cancers and liver diseases as leading causes of mortality, and again liver diseases as a major contributor of years of potential life lost (YPLL).

In Portugal, there are studies assessing the impact of specific digestive disorders: Marinho *et al* [36] addressed the rising costs and hospital admissions for hepatocellular carcinoma; and Cortez-Pinto *et al* [37] studied the burden and costs of diseases attributable to alcohol drinking.

Two other Portuguese studies evaluated the impact of liver diseases in hospitalization setting [38, 39]. Also Ramalho *et al* [40] and Antunes *et al*[22] studied the incidence and prevalence of celiac disease among pediatric Portuguese population.

In our study, we found evidence that digestive diseases represent an important and increasing burden for individuals, institutions and healthcare national service thus placing high demands in the future for healthcare organization. Globally, we found that the number of hospitalizations due to digestive diseases is increasing, older patients are being admitted, with higher costs and also higher mortality rates, what is significantly related to ageing of the population. Despite variability in hospitalization rate across the decade, with an increasing trend in the first five years followed by a decreasing trend afterwards, trends in charges and in-hospital mortality are showing unequivocal rising burden.

When adjusted to age, there were no significant changes through the decade both for monetary charges and for in-hospital mortality rates, what highlights the ageing of the population as a major contributor to trends in hospitalization indicators. Incidence and/or prevalence of many digestive diseases peak at older ages, and so it is likely that extended life expectancy will lead to future higher burden.

Although digestive diseases responsible for the largest number of hospitalizations are non-malignant diseases such as acute biliopancreatic disorders, digestive cancers still represent a major burden in hospitalization days, costs and mortality indicators, with a rising global trend profile. Upper and lower GI cancers contribute similarly to mortality (number of deaths), as opposed to USA where lower GI cancers are alone the first cause of digestive mortality[2].

Gastric cancer, known for high incidence and mortality in Portugal[41, 42, 43], often diagnosed in advanced stages of disease, requires special attention: although with a slight decrease in hospitalization rate over the decade, it still presents with the greatest number of in-hospital deaths of all digestive disorders.

Liver diseases, notably alcohol-related disorders and cirrhosis-related complications, are the principal cause of mortality in patients bellow 75 years old, representing therefore a crucial subject for future improvements. This is particularly important because the latest WHO report on health statistics demonstrates that Portugal is listed among the

countries with highest harmful consumption of alcohol worldwide[25, 39].

Biliary tract disease is a condition consuming great amount of healthcare resources given the number of hospitalization episodes, but with relatively low mortality. This finding is consistent with other reports[1, 2, 8, 44]. A likely explanation for this is again the ageing of the population, as well as the increasing prevalence of other risk factors such as obesity and diabetes.

Hospitalization for GI infections in the era of antibiotics misuse and widespread resistances poses an important concern. Even though the number of hospitalizations has decreased during the decade, mortality has increased, and so additional efforts in understanding the factors contribution to this trend might be of interest.

Assets and limitations of the study

Information collected using a database with national coverage allows reporting of burden of disease on a nationwide basis, strengthening the validity and credibility of the research. However, these depend largely on accuracy of diagnosis and procedures coding. Several studies have addressed this subject, studying the suitability of ICD coding in clinical research, finding them valid and accurate for several digestive diseases[31, 45, 46, 47], although in some reports combined databases or code combination are advised[48, 49, 50, 51].

A major strength of this study is reporting data on healthcare resource use and disease mortality over a time period of the decade 2000-2010, potentially serving as a valuable instrument for the current scrutiny and debate concerning the Portuguese healthcare service. We think these findings are representative of the Portuguese burden of digestive disease, but in addition may be of use in other European countries with similar healthcare organization, and current economic and social characteristics.

Some limitations to the present study should however be pointed out. Even though this study represents the totality of inpatient stays from public hospitals in Portugal, these represent 85% of all hospitalizations episodes, and so the real burden of digestive disease may be underestimated by missing the 15% inpatient episodes from private hospitals. We believe missing data from private hospitals could have further strengthened our findings. We were also not able to access healthcare indicators from primary care, urgent care or medication

consumption and costs, which might have contributed to underscoring the real growing burden of digestive diseases. Limitations on the use of ICD-9-CM coding are also noteworthy of mention, since underreporting is not so rare.

Challenges and opportunities for the future

In Portugal this health problem represents an important and increasing burden for individuals, institutions and healthcare national service thus placing high demands in the upcoming of healthcare organization. Our findings may be valuable to promote a wide reflection on the attention given to digestive diseases, from a broad range perspective and including several levels of care. Increasingly aged population, high prevalence of metabolic syndrome and persisting drinking habits are elements that anticipate no improvement in this disease burden. Particular diseases such as gastric cancer, biliary-tract disease and alcohol-related liver disorders should require special attention.

Proposed strategies for the future are: focus on information and prevention leading to risk reduction and patient engagement and also focus on improvement of palliative and end of life care. Transferring a part of care from classical hospitalization setting to ambulatory care setting, optimizing and maximizing resources such as day-hospital or minimal invasive procedures is already established in some Portuguese hospitals. Another challenging urgent investment in a rapidly ageing country like Portugal is the promotion of healthy ageing through political and social approaches leading to more active and healthy elderlies and making health and social services accessible, affordable and efficient particularly for them.

Future research on topics like health related quality of life, improvement of hospitalization outcomes, service planning and disease registries are likely to produce valuable information with future high applicability.

This reflection is of importance for decision makers, clinicians, researchers, payers and other stakeholders regarding resource allocation on future approaches and might represent a breakthrough in research, raising challenging new questions and possibilities.

5. Conclusion

In summary, we have demonstrated that digestive diseases represent an important burden in a southern European country such as Portugal, region where data on this subject are still lacking. This burden shows to be rising, as revealed through comparative analysis of indicators over the last decade, trends which are strongly related to ageing population. We found there are diseases source of particular concern, justifying a comprehensive close up in order to understand how to develop resources to improve outcomes. We expect that our research could be a cornerstone to a wide reflection on digestive diseases management, promoting multidisciplinary dialogue and effort.

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